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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/428,692	10/28/1999	DANIEL B. CARR	18475-016	4992

7590 12/17/2001

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EXAMINER	
LANDSMAN, ROBERT	
ART UNIT	**PAPER NUMBER**
1647	11

DATE MAILED: 12/17/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/428,692	Applicant(s) CARR ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Claims 1-23 are currently pending. Applicants have elected claims 1-17 as they read on SEQ ID NO:3 and 21. Since Applicants provide no traversal, this election is treated as an election without traverse. This restriction, therefore, is made FINAL.

2. Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 6-8, 11-13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

"**Fragments**" or "**derivatives**" of these binding moieties would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:2. Applicants provide no guidance or working examples of what amino acid residues can be added or deleted in order to maintain opioid and nociceptive moiety binding and function, nor would it be predictable to one of ordinary skill in the art how to alter either or both of these receptor moieties and maintain both binding and functional capabilities. The same is true for those claims reciting that the peptide has a "**D-amino acid**." Applicants have not discussed where this amino acid residue would occur, or how it would affect binding and function of these chimeras. Similarly, Applicants have not provided guidance or working examples of how they would be able to make and use a chimeric protein which has a

"**plurality**" of either opioid or nociceptive moieties, or both and which can still bind to, and function at, their specific receptors.

In summary, Applicants provide no guidance or working examples of how to make functional chimeras comprising derivatives or fragments of these moieties, including those comprising D-amino acids, or a plurality of moieties. These factors, along with the lack of predictability to one of ordinary skill in the art how to make these derivatives and fragments leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed. Claims 16 and 17 are rejected since they depend from rejected base claims.

3. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. "**Derivatives**" and "**fragments**" are proteins with one or more amino acid substitutions, deletions, insertions and/or additions to naturally occurring opioids and nociceptive binding moieties. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Tthe specification and claims do not provide any guidance as to what changes should be made in order to maintain the binding and functional characteristics of these moieties. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "opioid and nociceptive binding moiety" alone is insufficient to describe the genus. One of skill in the art would reasonably

conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

4. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kream et al (US Patent No. 5,891,842) in view of Cavagnero et al. (Life Sci 49:495-503, 1991) and further in view of Lappi et al. (US Patent No.6,063,758). The claims recite a chimeric peptide comprising an opioid receptor binding moiety and a nociceptive receptor binding moiety. The claims also recite moieties of specific SEQ ID NOs, pluralities, fragments and derivatives of these moieties as well as pharmaceutical compositions. Kream et al. teach that concurrent administration of marginal doses of opioids, including those that act at the mu opioid recepor, in combination with marginal doses of a nociceptive ligand, substance P (SP) produces a powerful potentiation and enhancement of an opioid response (Abstract; column 6, line 63 – column 7, line 18) in animals when administered as pharmaceutical compositions in vivo (column 7, line 1 – column 7, line 18; Figures 1-7). Kream et al. do not teach using these binding moieties as chimeric peptides.

However, Cavagnero et al. do teach that opioid peptides chimeras to produce analogs with specific characteristics. These compounds still bind to and activate opioid receptors in binding and functional assays (Abstract; Methods). Neither Kream et al. or Cavagnero et al. teach SP chimeras. However, Lappi et al. do teach SP, and analogs thereof, conjugated to Saporin as well as pharmaceutical compositions for the treatment of pain perception in a subject (Abstract; Figures 9A – 9E).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have substituted the DNA of the SP moiety of Lappi et al. in-frame into the vector of Cavagnero et al. for recombinant expression of an opioid/SP chimera as taught by Kream et al. Kream et al. teach that concurrent administration of marginal doses of opioids, including those that act at the mu opioid receptor, in combination with marginal doses of a nociceptive ligand, SP, produces a powerful potentiation and enhancement of an opioid response in animals when administered as pharmaceutical compositions in vivo. Lappi et al. also teach that SP chimeras can be used to inhibit pain perception in a subject.

Therefore, the artisan would have been motivated to produce a chimeric peptide comprising both an opioid receptor binding moiety and a nociceptive receptor binding moiety since both opioid and nociceptive peptide chimeras have been produced and have been shown to be functional. Therefore, it would have been expected that the artisan would have been successful in producing an opioid/SP chimera to treat pain in a subject.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
December 17, 2001

Gary L. Kunz
GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
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